PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
1336		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP 03/07514	12.06.2003	12.06.2002
International Patent Classification (IPC) or both national classification and IPC		
C12N15/00		
Applicant		
RIKEN		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.01.2004	01.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Fuchs, U Telephone No. +49 30 25901-321

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP 03/07514

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-87 as originally filed

Sequence listings part of the description, Pages

1-20 as originally filed

Claims, Numbers

1-55 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-35, 37-55
	No:	Claims	36
Inventive step (IS)	Yes:	Claims	7, 17-25
	No:	Claims	1-6, 8-16, 26-35, 37-55
Industrial applicability (IA)	Yes:	Claims	1-55
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 02 10438 A (JOHNS HOPKINS UNIVERSITY), 7 February 2002, cited in the application

D2: MARUYAMA, K. & SUGANO, S.: 'Oligo-capping: a simple method to replace the cap structure of eukaryotic mRNAs with oligoribonucleotides', GENE, vol. 138, no. 1-2, 28 January 1994, pages 171-174, cited in the application

D3: CARNINCI, P. & HAYASHIZAKI, Y.: 'High-Efficiency Full-Length cDNA Cloning', METHODS IN ENZYMOLOGY, vol. 303, 1999, pages 19-44, cited in the application

D4: EDERY, I. ET AL.: 'An Efficient Strategy To Isolate Full-Length cDNAs Based on an mRNA Cap Retention Procedure (CAPture)', MOLECULAR AND CELLULAR BIOLOGY, vol. 15, no. 6, June 1995, pages 3363-3371, cited in the application

D5: THEISSEN, H. ET AL.: 'Cloning of the human cDNA for the U1 RNA-associated 70K protein', EMBO JOURNAL, vol. 5, no. 12, 1 December 1986, pages 3209-3217, cited in the application

D6: EP-A-1 197 552 (RIKEN; HAYASHIZAKI, Y.), 17 April 2002, cited in the application

D7: US-B1-6 352 828 (BRENNER, S.), 5 March 2002, cited in the application

D8: WO 03 091416 A (LYNX THERAPEUTICS, INC.), 6 November 2003

1. Novelty (Article 33(2) PCT)

A sequence according to claim 36 derived from the concatemer prepared by a method according to claim 33 could be identical with a sequence already known in the prior art. However, a known sequence cannot be rendered novel and inventive, even if it would have been prepared by a novel and inventive method. Accordingly, the wording of **claim 36** is not acceptable.

2. Inventive Step (Article 33(3) PCT)

1.1 **D1** discloses a method for preparing long DNA tags derived from the ends of a mRNA comprising the steps of a) preparing a nucleic acid corresponding to a nucleotide sequence of one end of an mRNA , b) attaching at least one linker to the nucleic acid, c) cleaving the nucleic acid with a restriction enzyme ("tagging enzyme") having its recognition site within the linker and its cleavage site within the nucleic acid corresponding to the end of the mRNA (preferably *MmeI*, see page 15, paragraph 40) and d) collecting a resulting DNA fragment corresponding to the end of the mRNA (see page 10, paragraph 31; page 12, paragraph 34; page 14, paragraph 39 - page 15, paragraph 56 and pages 61-62, figure 1). Although the method is exemplified for obtaining 3'-end derived DNA tags, it is also proposed to be applicable for obtaining 5'-end derived DNA tags, "depending on which terminus is used for capture" (see page 10, paragraph 31). Especially the use of the 5'-cap of a transcript which "can be utilized for labelling or binding a capture means for isolation of a 5' defined sequence tag" is suggested (see page 12, lines 7-11). In other words, the strategy of the method of claim 1 has been already disclosed in D1. Therefore, in view of D1, the subject-matter of **claim 1** and **dependent claims 2-5, 8, 11, 26-29, 33-35, 37-55** is not considered as involving an inventive step.

1.2 With the knowledge of D1 in combination with the following documents, the specific embodiments of claim 1 as claimed in the dependent claims are also not considered to involve an inventive step. **D2** reports a method designated oligo-capping corresponding to the embodiment of **claim 6** and **D3** described a method designated cap-trapper relating to the embodiment of **claims 12, 14, 15 and 16.** In **D4 and D5** methods for selecting a particular cDNA/RNA hybrid that has the 5' cap structure of the mRNA using a selective binding substance which specifically recognizes the 5' cap

structure are presented according to the embodiment of **claims 9, 10, 13 and 16. D6** discloses a method of normalization and/or substraction of first-strand cDNA according to **claims 30 and 31** and **D7** discloses a method of large-scale parallel sequencing of tags involving a step of attaching the collected nucleic acids to beads according to **claim 32.**

3. Certain Published Document (Rule 70.10 PCT)

D8 relates to a method for preparing long DNA tags derived from the 5'-ends of mRNAs involving ligation of linkers containing recognition sites for class IIS restriction endonucleases having their cleavage site located in the DNA derived from the 5'-end of the mRNA. The content of D8 could be relevant for assessing novelty of the subject-matter of claims 1 and 7 and of the dependent claims.

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 03 091416	06/11/2003	25/04/2003	26/04/2002